

USTUR WHOLE BODY CASE 0262: 33-Y FOLLOW-UP OF PUO₂ IN A SKIN WOUND AND ASSOCIATED AXILLARY NODE

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Abstract — This whole body donation case (USTUR Registrant) involved two suspected PuO₂ inhalation intakes, each indicated by a measurable Pu α -activity in a single urine sample, followed about 1½ y later by a puncture wound to the thumb while working in a Pu glovebox. The study is concerned with modeling simultaneously the biokinetics of deposition and retention in the respiratory tract and at the wound site; and the biokinetics of Pu subsequently transferred to other body organs, until the donor's death. Urine samples taken after the wound incident had readily measurable Pu α -activity over the next 14 y, before dropping below the minimum detectable excretion rate (< 0.4 mBq d⁻¹). The Registrant died about 33 y after the wound intake, at age 71 y, from hepatocellular carcinoma with extensive metastases. At autopsy, all major soft tissue organs were harvested for analysis of their ²³⁸Pu, ²³⁹⁺²⁴⁰Pu and ²⁴¹Am content. The amount of ²³⁹⁺²⁴⁰Pu retained at the wound site was 68 ± 7 Bq (1 S.D.), measured by low-energy planar Ge (LEGe) spectrometry. A further 56.0 ± 1.2 Bq was retained in an associated axillary lymph node, measured by radiochemistry. Simultaneous mathematical analysis (modeling) of all *in vivo* urinary excretion data, together with the measured lung, thoracic lymph node, wound, axillary lymph node, and systemic tissue contents at death, yielded estimated intake amounts of 757 and 1,504 Bq, respectively, for the first and second inhalation incidents, and 204 Bq for the total wound intake. The inhaled Pu material was highly insoluble, with an estimated long-term absorption rate from the lungs of 2 × 10⁻⁵ d⁻¹. The Pu material deposited at the wound site was mixed: about 14% was rapidly absorbed, about 49% was absorbed at the rate of about 6 × 10⁻⁵ d⁻¹, and the remainder (about 37%) was absorbed extremely slowly (at the rate of about 5 × 10⁻⁶ d⁻¹). Thus, it was estimated that only about 40% of the Pu initially deposited in the wound had been absorbed systemically over the 33-y period until the donor's death. The biokinetic modeling also indicated that, in this individual case, some of the parameter values (rate constants) incorporated in the ICRP Publication 67 Pu model were up to a factor two different from ICRP's recommended values (for Reference Man).

INTRODUCTION

The United States Transuranium and Uranium Registries (USTUR) maintains an extensive and growing data base of health physics information and measured actinide content of tissues for former workers who were known to have had intakes of actinide elements during their employment in the nuclear industry. These registrants had volunteered to donate tissues after their death for radiochemical analyses and biokinetic modeling studies. Case 0262, the subject of this study, is of particular interest since his intakes were well documented, and they occurred as two discrete (acute) inhalation events, with a further intake *via* a cutaneous puncture wound. Case 0262 is a whole body donation, for whom USTUR has analysed radiochemically the contents of ²³⁹⁺²⁴⁰Pu in all major soft tissue organs and individual bones comprising about half the skeleton, plus ²³⁸Pu and ²⁴¹Am. The ²³⁸Pu and ²⁴¹Am data, and biokinetic

modeling of ²⁴¹Am in-growth in tissues from ²⁴¹Pu decay of the Pu material taken into the body will be reported elsewhere. This paper is concerned with modeling the systemic uptakes of Pu from both inhalations and the wound, and the subsequent long-term tissue retention of Pu.

THE DONOR

This gentleman worked as an engineer at the Hanford site, from 1951-82. He died in 1990, at age 71 y, from hepatocellular carcinoma with metastases to the diaphragm, lungs and liver. Incidental autopsy findings included degenerative arthritis of hip and shoulder joints, and diffuse degenerative changes of the lumbar spine (indicative of osteoporosis). At autopsy, the skin was taken from both hands in order to examine both for residual actinide activity, together with the axillary lymph node associated with the left hand. The skin wound occurred on the left thumb.

Health Physics/Incident Data

In 1956, this worker had two suspected intakes of nominally 'fresh' weapons grade Pu. In the first incident, with no respiratory protection worn, a substantial airborne Pu concentration was detected. In the second incident, two weeks later, both hands were heavily contaminated (exceeding 10,000 dpm α -activity). Urine samples taken promptly after both incidents had measurable Pu α -activity. However, subsequent urine samples had no measurable Pu α -activity (< 0.025 dpm per 24-h sample). The Pu urinalysis method⁽¹⁾ was (i) separation of the ^{241}Pu contaminant by lanthanum fluoride precipitation and thenoyl trifluoroacetone (TTA) extraction of plutonium, (ii) electrodeposition of the Pu isotopes on a stainless steel disk, and (iii) counting of total α -activity using nuclear track emulsion autoradiography (α -track counting).

The third intake (Pu wound to left thumb) occurred about 500 d later, when a broken drill bit punctured the worker's left glove while he was working in a glove box. The initial external count rate at the wound site, measured by α -probe, was about 500 cpm. There was no general airborne release, but the glove involved in the incident was highly contaminated with about 40,000 dpm (667 Bq) of α -activity.

Wound and Medical Management

Medical findings were a 1/4-inch laceration (1/8-inch deep) on the terminal phalanges of the left thumb with little or no bleeding. A suction cup was applied and about 2 mL of fluid was obtained. There was apparently no α -activity above background in the fluid removed, but information about the detection method used is not available. The initial count rate from the wound site was reduced somewhat by washing the skin with a decontamination agent, but there was no mention in the dosimetry records of subsequent chelation therapy or surgical removal of tissue.

At about 7 y after the wound intake, the registrant's employer estimated that his total lifetime systemic uptake of plutonium would be approximately 2.3 nCi (84 Bq) of Pu (primarily $^{239+240}\text{Pu}$) contaminated with 18 nCi (660 Bq) of ^{241}Pu . This corresponded to about 15% of the contemporary 'maximum permissible body burden' (MPBB)⁽²⁾. The estimated Pu uptake was derived from graphical analysis of the Pu-in-urine bioassay data, using the Langham⁽³⁾ power function to resolve the component of systemic uptake due to initially 'soluble' plutonium, i.e., that absorbed within days, and the Healy⁽⁴⁾ method for the component from initially 'insoluble' or slowly absorbed plutonium. The relative amount of ^{241}Pu was estimated from an assumed isotopic ratio of the source material.

AUTOPSY TISSUE DATA**Skin and Wound Site**

The skin of the left thumb (containing the wound site) was not analysed radiochemically. This has been preserved for α -particle autoradiography and histological study. The total $^{239+240}\text{Pu}$ and ^{241}Am contents were measured by photon spectrometry using a low-energy planar Ge (LEGe) detector. The skin sample, approximately 0.5 cm thick, was prepared by stretching it on a flat surface and counting successively with the inner and outer surface facing the LEGe detector, at distances of 1.5 and 4 inch. The emission rate for 17-keV X-rays was approximately equal from the inner and outer surfaces of the skin, indicating a mid-depth location of the Pu source material. An appropriate correction was made for self absorption in the overlying tissue.

Other Tissues

Table 1 gives a summary of the total $^{239+240}\text{Pu}$ activity measured (by radiochemical analysis) in major organs and the left axillary lymph node (associated with the left thumb wound). The full radiochemical analysis results (^{238}Pu , $^{239+240}\text{Pu}$ and ^{241}Am) measured in all sampled tissues (including individual bones) can be downloaded from <http://www.ustur.wsu.edu/Montpellier/index.html>.

Table 1. Measured $^{239+240}\text{Pu}$ tissue contents

Organ/Tissue	Activity at Death, Bq
Wound site (left thumb)	68 ± 7 (1 σ)
Left axillary lymph node	56.0 ± 1.2 (1 σ)
Lungs, larynx, trachea	2.6
Thoracic lymph nodes (LNTH)	1.1
Skeleton	29.1
Liver	20.7
Kidneys	0.053
Testes	0.018
All other soft tissues (total)	8.6
Spleen	3.1
Brain	0.067
Stomach wall	0.44
Small intestine wall	0.056
Large intestine wall	0.008
Total 'Systemic'	52.2

DATA ANALYSIS AND RESULTS

The software package IMBA Expert™ USDOE-Edition⁽⁵⁾ was used first to derive the amounts and characteristics of the two initial intakes by inhalation, and the amount of total Pu α-activity deposited in the skin puncture wound together with its subsequent rate(s) of absorption into the blood. This software implements the ‘Human Respiratory Tract Model’ (HRTM) of ICRP Publication 66⁽⁶⁾ as applied for the ICRP Publication 68⁽⁷⁾ Reference Worker. The uptake and retention of Pu in the major body organs, and the excretion in urine and faeces, is represented by the ICRP Publication 67⁽⁸⁾ biokinetic model for Pu (IC67). The software does not distinguish between material retained at the wound site and that translocated (as particles) to an associated lymph node. Instead, all particulate activity that was initially deposited in the ‘wound’ is treated as material in one or more ‘extra-systemic’ compartments. These compartments are assumed to release Pu at a constant rate, by the process of dissolution and absorption of Pu into the blood. Thus, the total ‘extra-systemic’ retention of Pu at the wound site and/or any associated lymph nodes is represented by the sum of one or more exponentially cleared compartments.

Given the observed bioassay data and a specific set of assumptions about the characteristics of any intakes, the IMBA Expert™ software applies the ‘maximum likelihood method’ to evaluate simultaneously the most likely amounts of each intake⁽⁹⁾. The maximum likelihood method enables appropriate statistical weight to be applied to data values recorded as ‘less than the limit of detection’ (<LOD), as are present in both the early urinary

excretion data for this case, and that beyond 14 y. The error distribution for the urine data was assumed to be lognormal, where the associated value of σ_g was determined empirically to reflect the observed ‘scatter’ in sequential data points.

The ‘best fit’ values of absorption rates, and other model parameters were found by minimising the calculated value of the χ^2 -sum, with the fitted parameter values constrained to predict exactly the measured lung, thoracic lymph node, and whole body activity (Table 1). The whole body activity included the residual amounts of Pu measured at death in the skin wound and the associated axillary lymph node. These initial estimates from The IMBA Expert™ analysis are shown in Table 2.

Table 2. IMBA Expert™ analysis results

Intake Component	Amount, Bq	Absorption Rate(s), d ⁻¹
<u>Inhalations:</u>		
#1	450	$s_p = 0.2; s_t = 2 \times 10^{-5}$
#2	1,811	$s_p = 0.2; s_t = 2 \times 10^{-5}$
<u>Wound:</u>		
#1	6.4	0.5
#2	23.4	0.012
#3	166	5×10^{-5}

The ‘IMBA’ estimates were used as initial values to carry out a more comprehensive analysis of the specific values of dominant rate constants in the IC67 Pu biokinetic model that are applicable for this individual donor, as described below.

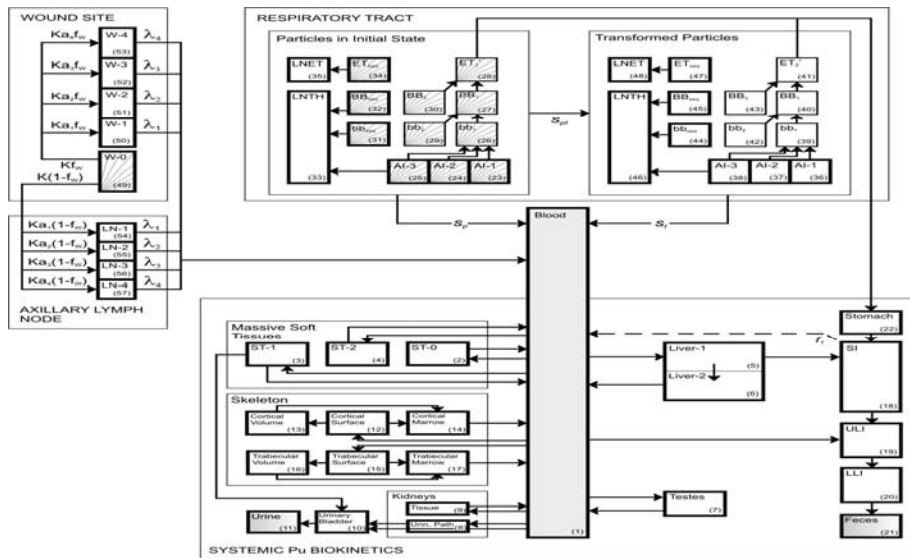


Figure 1. Composite inhalation/wound biokinetic system.

The combined wound, axillary lymph node and systemic Pu model system shown in Figure 1 was solved analytically in successive time-steps corresponding to the three intake events, all urine sampling intervals, and the time of death, using the 'rate matrix' method^(10,11). The rate matrix was solved iteratively, using the 'grid-search' method⁽¹²⁾ to find the combination of trial parameter values that minimises the calculated value of $\Sigma\chi^2_{\text{urine}}$. This analysis was performed twice: (i) with all rate constants in the IC67 Pu biokinetic model set to ICRP's recommended values, and (ii) also varying iteratively the systemic Pu model parameter values which minimise $\Sigma\chi^2_{\text{total}}$, i.e., provide a simultaneous exact fit to the measured organ contents ($\Sigma\chi^2_{\text{organ}} = 0$). Figure 2 shows the corresponding best fits to the urine bioassay data so obtained.

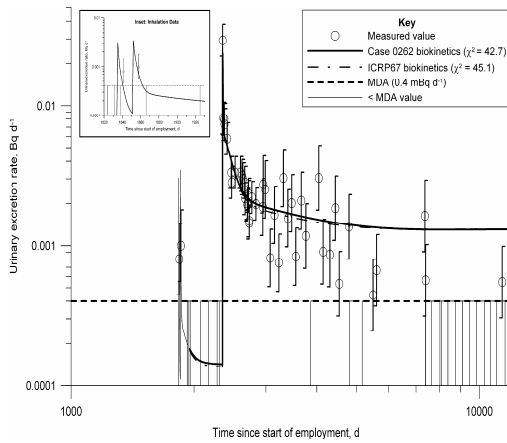


Figure 2. Minimised $\Sigma\chi^2$ fits to the urine bioassay data compared for reference and modified IC67 Pu biokinetic model.

Note that the ICRP-recommended Pu biokinetic model parameter values give almost as good a 'fit' to the urine data ($\Sigma\chi^2_{\text{urine}} = 45.1$) as the case-specific values 'optimised' to fit to the measured organ contents ($\Sigma\chi^2_{\text{urine}} = 42.7$).

Table 3 shows the resulting 'best fit' to the measured tissue contents obtainable with all ICRP-recommended parameter values in the Pu systemic model, together with modified parameter values in the HRTM (IC66). Optimisation of the critical parameter values in the IC67 systemic Pu model reduced all of the residual 'error' values shown in Table 3 to zero, i.e., predicted exactly the measured organ contents. Table 4 shows the modifications to ICRP's reference parameter values (multiplying factors) needed to match the organ contents measured in this individual whole body donor.

Table 3. 'Best fit' tissue contents predicted by IC67 Pu biokinetics with IC66 parameter values optimised for Case 0262

Tissue	Content of $^{239+240}\text{Pu}$, Bq		
	Measured	IC67 Model	Error, %
Wound	68.0	68.0	0
Axillary lymph node	56.0	56.0	0
Lung	2.59	2.59	0
Thoracic lymph nodes	1.05	1.05	0
Skeleton	29.1	33.2	+14
Trabecular bone	17.6	9.2	-48
Cortical bone	11.5	24.0	+109
Red bone marrow	-	0.82	-
Liver	20.7	20.0	-3
Massive soft tissues	8.6	5.3	-38
Testes	0.018	0.025	+39
Kidneys	0.053	0.061	+15

Table 4. Optimised IC66/67 parameter values for Case 0262

Transfer Pathway	Transfer Rate, d^{-1}	
	IC66/67 Reference Value	Case 0262 Factor
Respiratory tract (IC66):		
A13 to bb1	0.0001	$\times 0.918$
A13 to LNTH	0.00002	$\times 0.526$
Systemic Pu model (IC67):		
Blood to Cortical bone surface	0.3235×0.4	$\times 0.444$
Cortical bone volume to Marrow	0.0000821	$\times 0.53$
Blood to Trabecular bone surface	0.3235×0.6	$\times 1.133$
Trabecular bone surface to Volume	0.000247	$\times 1.40$
Trabecular bone volume to Marrow	0.000493	$\times 0.35$
Trabecular marrow to Blood	0.0076	$\times 0.605$
Blood to Liver 1	0.1941	$\times 0.928$
Liver 2 to Blood	0.000211	$\times 0.90$
Blood to Other kidney tissue	0.00323	$\times 0.827$
Blood to Urinary path	0.00647	$\times 0.90$
Blood to Urinary bladder content	0.0129	$\times 0.90$
Blood to ST-2	0.0129	$\times 1.84$
Blood to Testes	0.00023	$\times 0.69$

Derived characteristics of inhaled Pu material

The urinary excretion pattern shown in Figure 2 (inset) is not consistent with that predicted by the ICRP default parameters for insoluble Pu (Type S). The following case-specific parameter values were found to predict both the measured total lung burden of $^{239+240}\text{Pu}$ at death (3.64 Bq at 12,536 d after the first inhalation intake) and the measured LNTH burden of 1.05 Bq,

while simultaneously minimizing the value of $\Sigma\chi^2_{\text{urine}}$ and fitting exactly the measured ²³⁹⁺²⁴⁰Pu contents of major organs:

- Intake(1) = 757 Bq, Intake (2) = 1,504 Bq (assuming a 5- μm -AMAD aerosol).
- $\lambda_{\text{sp}} = 0.2 \text{ d}^{-1}$, $\lambda_{\text{spt}} = 100 \text{ d}^{-1}$, $\lambda_{\text{st}} = 2 \times 10^{-5} \text{ d}^{-1}$.
- No bound material.

Derived wound/axillary node intake and retention

- Total intake = 204 Bq
- Wound retention at death (12,021 d; 32.9 y) = 68 Bq.
- Axillary lymph node retention = 56 Bq.
- Fractional absorption rates:
 - $\lambda_1 = 0.5 \text{ d}^{-1}$ (3.3%);
 - $\lambda_2 = 0.012 \text{ d}^{-1}$ (10.3%);
 - $\lambda_3 = 5.9 \times 10^{-5} \text{ d}^{-1}$ (49.1%);
 - $\lambda_4 = 5 \times 10^{-6} \text{ d}^{-1}$ (37.4%).

There was no visible scarring of the skin (wound site) containing this Pu material.

The analysis carried out here (with the wound/lymph node biokinetic model structure shown in Figure 1) assumes rapid initial partitioning of deposited particles (by lymphatic flow) between the wound site and axillary node, where the partition fraction is assumed to be defined by the ratio of node : wound activity measured at autopsy. Thus, the time-dependent absorption rates are assumed to be identical for particles retained at the wound site and those transferred to the axillary node. The actual rate of lymphatic transfer to the axillary node cannot be resolved from the urine bioassay and autopsy tissue data alone.

The observed multi-phased wound/lymph node retention characteristics indicate that the Pu contamination in the glove box consisted predominantly of highly insoluble PuO₂ mixed with about 14% of ‘soluble’ Pu.

Organ/tissue contents predicted as a function of time

Figure 3 shows the temporal pattern of uptake by systemic organs predicted by the modified IC66/67 model parameters (Table 4) in this case, in comparison with the respective organ contents measured at autopsy. With the predominant, very slow uptake of Pu from the wound and axillary lymph node, the maximum amount of total ‘systemic’ activity occurred at the end of life (34 y after the first inhalation intake), i.e., the maximum ‘body burden’ is that directly measured at autopsy.

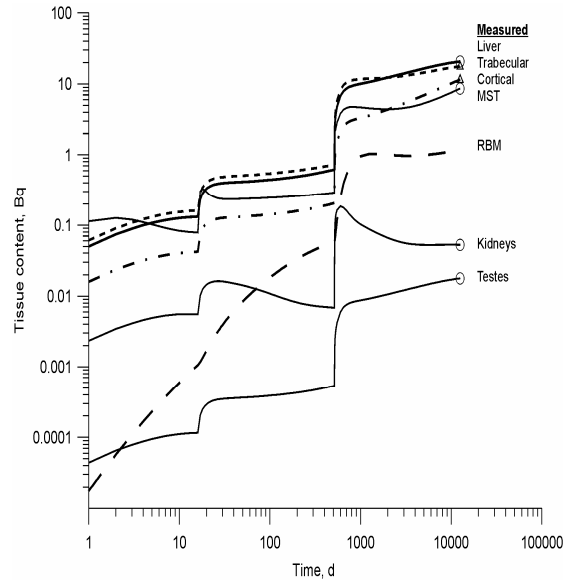


Figure 3. Predicted temporal uptake of Pu in systemic organs with values measured at autopsy.

Thus, the maximum total systemic activity measured in this case is 52 Bq (1.4 nCi), where this includes the activity measured in the lungs and thoracic lymph nodes, but excludes that retained in the skin wound and axillary lymph node. Applying the IC67 Pu biokinetic model for the Reference Worker (and the ICRP Publication 60 tissue weighting factors)⁽¹³⁾, the effective dose (resulting from the ²³⁹⁺²⁴⁰Pu in these three intakes) is approximately 35 mSv (3.5 rem).

CONCLUSIONS AND COMMENT

The fitted long-term absorption rate of $2 \times 10^{-5} \text{ d}^{-1}$ for the Pu material inhaled in this case (presumed to be PuO₂) is one-fifth of ICRP’s recommended default value for Type S (of 10^{-4} d^{-1}). In conjunction with this slower absorption rate, the fitted rate of particle transfer to the thoracic lymph nodes (AI3→LNTH pathway) is about half the ICRP default value of $2 \times 10^{-5} \text{ d}^{-1}$. The long (33-y) follow-up of this USTUR whole body donor has enabled the extremely slow absorption of PuO₂ from a skin puncture wound to be observed. In this case, only about one-quarter of the initially deposited ‘insoluble’ material was absorbed into the blood. Only relatively small changes to some of ICRP’s recommended parameter values in the Pu biokinetic model were necessary to predict exactly the tissue contents of Pu measured at autopsy. However, these autopsy measurements showed greater than predicted retention in trabecular bone with relatively lower retention in cortical bone.

In the authors' opinion, this case demonstrates the remarkable skill, judgement and 'prescience' of the 1950s site pre-health physicists and medical practitioners, who, on the basis of limited contemporary knowledge and primitive computational tools, succeeded in predicting this gentleman's total systemic Pu content (measured three decades later) to within a factor of 2!

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